

Q-1 SUB B1 CONC
FISYDGSNKHYADSVKG (SEQ ID NO:33) and TGWLGPFDY (SEQ ID NO: 37), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQSVSSSFLA (SEQ ID NO:25), GASSRAT (SEQ ID NO:30), and QQYGSSPWT (SEQ ID NO:35), respectively.

✓
Please replace the paragraph beginning on page 7, line 13, with the following amended paragraph:

Q-2 SUB B2
Other human sequence antibodies of the invention comprise heavy chain CDR1, CDR2, and CDR3 sequences, SYGMH (SEQ ID NO:28), VIWYDGSNKYYADSVKG (SEQ ID NO:34) and APNYIGAFDV (SEQ ID NO:38), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQGISSWLA (SEQ ID NO:26), AASSLQS (SEQ ID NO:31), and QQYNSYPPT (SEQ ID NO:36), respectively.

✓
Please replace the paragraph beginning on page 8, line 3, with the following amended paragraph:

Q-3 SUB B3
The invention provides a hybridoma cell line comprising a B cell obtained from a transgenic non-human animal having a genome comprising a human sequence heavy chain transgene and a human sequence light chain transgene, wherein the hybridoma produces a human sequence antibody that specifically binds to human CTLA-4. In a related embodiment, the hybridoma secretes a human sequence antibody that specifically binds human CTLA-4 or binding fragment thereof, wherein the antibody is selected from the group consisting of: a human sequence antibody comprising heavy chain heavy chain CDR1, CDR2, and CDR3 sequences, SYTMH (SEQ ID NO:27), FISYDGNKYYADSVKG (SEQ ID NO:32) and TGWLGPFDY (SEQ ID NO:37), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQSVGSSYLA (SEQ ID NO:24), GAFSRAT (SEQ ID NO:29), and QQYGSSPWT (SEQ ID NO:35), respectively, and heavy chain and light chain variable region amino acid sequences as set forth in SEQ ID NO:17 and SEQ ID NO:7, respectively; a human sequence antibody comprising heavy chain CDR1, CDR2, and CDR3 sequences, SYTMH (SEQ ID NO:27), FISYDGSNKHYADSVKG

and ligated to transcription promoter sequences to create a functional minigene for transfection into cells.

Please replace the paragraph beginning on page 76, line 23, with the following amended paragraph:

The gamma1 heavy chain plasmid, pCG7-96 (SEQ ID NO:40), includes the human gamma1 constant region and polyadenylation site, such that gamma sequences amplified with 5' primers that include HindIII sites upstream of the initiator methionine can be digested with HindIII and AgeI, and cloned into pCG7-96 digested with HindIII and AgeI to reconstruct a complete gamma1 heavy chain coding sequence together with a polyadenylation site. This cassette can be isolated as a HindIII/SalI fragment and ligated to transcription promoter sequences to create a functional minigene for transfection into cells.

Please replace the paragraph beginning on page 76, line 31, with the following amended paragraph:

The gamma4 heavy chain plasmid, pG4HE (SEQ ID NO:41), includes the human gamma4 constant region and polyadenylation site, such that gamma sequences amplified with 5' primers that include HindIII sites upstream of the initiator methionine can be digested with HindIII and AgeI, and cloned into pG4HE digested with HindIII and AgeI to reconstruct a complete gamma4 heavy chain coding sequence together with a polyadenylation site. This cassette can be isolated as a HindIII/EcoRI fragment and ligated to transcription promoter sequences to create a functional minigene for transfection into cells.

Please insert the following paragraph immediately before the paragraph beginning at page 93, line 1 of the specification:

SEQ ID NO:1 pGP1k

AATTAGCGGC CGCTGTCGAC AAGCTTCGAA TTCAGTATCG ATGTGGGGTA	50
CCTACTGTCC CGGGATTGCG GATCCGCGAT GATATCGTTG ATCCTCGAGT	100
GCGGCCGCAG TATGCAAAAA AAAGCCCCCT CATTAGGCGG GCTCTTGGCA	150
GAACATATCC ATCGCGTCCG CCATCTCCAG CAGCCGCACG CGGCGCATCT	200
CGGGCAGCGT TGGTCTCTGG CCACGGGTGG GCATGATCGT GCTCCTGTCTG	250

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SUB
B & end 161

GTTCCGCGCA CATTTCCTCCG AAAAGTGCCA CCTGACGTCT AAGAAACCAT 3100
TATTATCATG ACATTAACCT ATAAAAATAG GCGTATCACG AGGCCCTTTC 3150
GTCTTCAAG 3159

Please replace the paragraph beginning on page 93, line 1, with the following amended paragraph:

Q/7
SUB
B9

pCK7-96 (Nucleotide residues 3376 to 3881)(SEQ ID NO:39)

AGGAGAATGAATAAAATAAAGTGAATCTTTGCACCTGTGGTTTCTCTCTTTCCTCAATTTAATAATTATT
ATCTGTTGTTTACCAACTACTCAATTTCTCTTATAAGGGACTAAATATGTAGTCATCCTAAGGCGCATA
ACCATTATATAAAAAATCATCCTTCATTCTATTTACCTATCATCCTCTGCAAGACAGTCCTCCCTCAAA
CCCACAAGCCTTCTGTCTCACAGTCCCCTGGGCCATGGATCCTCACATCCCAATCCGCGGCCGCAATT
CGTAATCATGGTCATAGCTGTTTCTGTGTGAATTGTTATCCGCTCACAATCCACACAACATACGAG
CCGGAAGCATAAAGTGTAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCT
CACTGCCCGCTTTCAGTCGGGAAACCTGTCTGTCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGA
GAGGCGGTTTGCGTATTGGGCGC

Please replace the paragraph beginning on page 93, line 8, with the following amended paragraph:

SJB
B10

pCG7-96 (SEQ ID NO:40)

Please replace the paragraph beginning on page 94, line 12, with the following amended paragraph:

SJB
B11

pG4HE (SEQ ID NO:41)

Please replace the paragraph beginning on page 95, line 17, with the following amended paragraph:

Q/8
SUB
B12

10D1 VH(SEQ ID NO:16)

Please replace the paragraph beginning on page 95, line 27, with the following amended paragraph:

Q/9
SUB
B13

10D1 VK(SEQ ID NO:6)

Please replace the paragraph beginning on page 95, line 37, with the following amended paragraph:

Q/10
SUB
B14

4B6 VH(SEQ ID NO:18)

The following new paragraph has been inserted immediately before the paragraph beginning on page 93, line 1, of the specification:

SEQ ID NO:1 pGP1k

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AATTAGCGGC CGCTGTCGAC AAGCTTCGAA TTCAGTATCG ATGTGGGGTA 50
CCTACTGTCC CGGGATTGCG GATCCGCGAT GATATCGTTG ATCCTCGAGT 100
GCGGCCGCAG TATGCAAAAA AAAGCCCGCT CATTAGGCGG GCTCTTGGA 150
GAACATATCC ATCGCGTCCG CCATCTCCAG CAGCCGCACG CGGCGCATCT 200
CGGGCAGCGT TGGGTCCTGG CCACGGGTGC GCATGATCGT GCTCCTGTCTG 250
TTGAGGACCC GGCTAGGCTG GCGGGGTTCG CTTACTGGTT AGCAGAATGA 300
ATCACCGATA CGCGAGCGAA CGTGAAGCGA CTGCTGCTGC AAAACGTCTG 350
CGACCTGAGC AACACATGA ATGGTCTTCG GTTTCGCGTGT TTCGTAAAGT 400
CTGGAAACGC GGAAGTCAGC GCCCTGCACC ATTATGTTCC GGATCTGCAT 450
CGCAGGATGC TGCTGGCTAC CCTGTGGAAC ACCTACATCT GTATTAACGA 500
AGCGCTGGCA TTGACCCTGA GTGATTTTTC TCTGGTCCCG CCGCATCCAT 550
ACCGCCAGTT GTTTACCCTC ACAACGTTCC AGTAACCGGG CATGTTTCATC 600
ATCAGTAACC CGTATCGTGA GCATCCTCTC TCGTTTCATC GGTATCATTA 650
CCCCCATGAA CAGAAATTCC CCCTTACACG GAGGCATCAA GTGACCAAAC 700
AGGAAAAAAC CGCCCTTAAC ATGGCCCGCT TTATCAGAAG CCAGACATTA 750
ACGCTTCTGG AGAAACTCAA CGAGCTGGAC GCGGATGAAC AGGCAGACAT 800
CTGTGAATCG CTTACGACC ACGCTGATGA GCTTTACCGC AGCTGCCTCG 850
CGCGTTTCGG TGATGACGGT GAAAACCTCT GACACATGCA GCTCCCGGAG 900
ACGGTCACAG CTTGTCTGTA AGCGGATGCC GGGAGCAGAC AAGCCCGTCA 950
GGGCGCGTCA GCGGGTGTTG GCGGGTGTCG GGGCGCAGCC ATGACCCAGT 1000
CACGTAGCGA TAGCGGAGTG TATACTGGCT TAACTATGCG GCATCAGAGC 1050
AGATTGTAAT GAGAGTGCAC CATATGCGGT GTGAAATACC GCACAGATGC 1100
GTAAGGAGAA AATACCGCAT CAGGCGCTCT TCCGCTTCCT CGCTCACTGA 1150
CTCGTGCAGC TCGGTCGTTT GGCTGCGGCG AGCGGTATCA GCTCACTCAA 1200
AGGCGGTAAT ACGGTTATCC ACAGAATCAG GGGATAACGC AGGAAAGAAC 1250
ATGTGAGCAA AAGGCCAGCA AAAGGCCAGG AACCCTAAAA AGGCCGCGTT 1300
GCTGGCGTTT TTCCATAGGC TCCGCCCCCC TGACGAGCAT CACAAAAATC 1350
GACGCTCAAG TCAGAGGTGG CGAAACCCGA CAGGACTATA AAGATACCAG 1400
GCGTTTCCCC CTGGAAGCTC CCTCGTGCGC TCTCCTGTTT CGACCCTGCC 1450
GCTTACCGGA TACCTGTCCG CCTTCTCCC TTCGGGAAGC GTGGCGCTTT 1500
CTCATAGCTC ACGCTGTAGG TATCTCAGT CGGTGTAGGT CGTTCGCTCC 1550
AAGCTGGGCT GTGTGCACGA ACCCCCGTT CAGCCCGACC GCTGCGCCTT 1600
ATCCGGTAAT TATCGTCTG AGTCCAACCC GGTAAGACAC GACTTATCGC 1650
CACTGGCAGC AGCCAGGCGC GCCTTGGCCT AAGAGGCCAC TGTAACAGG 1700
ATTAGCAGAG CGAGGTATGT AGGCGGTGCT ACAGAGTTCT TGAAGTGGTG 1750
GCCTAACTAC GGCTACACTA GAAGGACAGT ATTTGGTATC TGCGCTCTGC 1800
TGAAGCCAGT TACCTTCGGA AAAAGAGTTG GTAGCTCTTG ATCCGGCAA 1850
CAAACCACCG CTGGTAGCGG TGGTTTTTTT GTTTGCAAGC AGCAGATTAC 1900
GCGCAGAAAA AAAGGATCTC AAGAAGATCC TTTGATCTTT TCTACGGGGT 1950
CTGACGCTCA GTGGAACGAA AACTCACGTT AAGGGATTTT GGTCAATGAGA 2000
TTATCAAAAA GGATCTTCAC CTAGATCCTT TTAATTAATA AATGAAGTTT 2050
TAAATCAATC TAAAGTATAT ATGAGTAAAC TTGGTCTGAC AGTTACCAAT 2100
GCTTAATCAG TGAGGCACCT ATCTCAGCGA TCTGTCTATT TCGTTCATCC 2150
ATAGTTGCCT GACTCCCCGT CGTGTAGATA ACTACGATAC GGGAGGGGCTT 2200
ACCATCTGGC CCCAGTGCTG CAATGATACC GCGAGACCCA CGCTACCCGG 2250
CTCCAGATTT ATCAGCAATA AACCAGCCAG CCGGAAGGGC CGAGCGCAGA 2300
AGTGGTCTTG CAACTTTATC CGCCTCCATC CAGTCTATTA ATTGTTGCCG 2350
GGAAGCTAGA GTAAGTAGTT GCCAGTTAA TAGTTTGCGC AACGTTGTTG 2400
CCATTGCTGC AGGCATCGTG GTGTACGCT CGTCGTTTGG TATGGCTTCA 2450
TTCAGCTCCG GTTCCCAACG ATCAAGGCGA GTTACATGAT CCCCCATGTT 2500
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GTGCAAAAAA GCGGTTAGCT CCTTCGGTCC TCCGATCGTT GTCAGAAGTA 2550
AGTTGGCCGC AGTGTTATCA CTCATGGTTA TGGCAGCACT GCATAATTCT 2600
CTTACTGTCA TGCCATCCGT AAGATGCTTT TCTGTGACTG GTGAGTACTC 2650
AACCAAGTCA TTCTGAGAAT AGTGTATGCG GCGACCGAGT TGCTCTTGCC 2700
CGGCGTCAAC ACGGGATAAT ACCGCGCCAC ATAGCAGAAC TTTAAAAGTG 2750
CTCATCATTG GAAAACGTTT TCGGGGCGA AAACCTCTCA GGATCTTACC 2800
GCTGTTGAGA TCCAGTTCGA TGTAACCCAC TCGTGACCCC AACTGATCTT 2850
CAGCATCTTT TACTTTCACC AGCGTTTCTG GGTGAGCAAA AACAGGAAGG 2900
CAAAATGCCG CAAAAAAGGG AATAAGGGCG ACACGGAAAT GTTGAATACT 2950
CATACTCTT CTTTTCAAT ATTATTGAAG CATTTATCAG GGTTATTGTC 3000
TCATGAGCGG ATACATATTT GAATGTATTT AGAAAAATAA ACAAATAGGG 3050
GTTCCGCGCA CATTTCCCCG AAAAGTGCCA CCTGACGTCT AAGAAACCAT 3100
TATTATCATG ACATTAACCT ATAAAAATAG GCGTATCACG AGGCCCTTTC 3150
GTCTTCAAG 3159

The paragraph beginning on page 93, line 1, has been amended as follows:

pCK7-96 (Nucleotide residues 3376 to 3881)(SEQ ID NO:39)

AGGAGAATGAATAAAATAAAGTGAATCTTTGCACCTGTGGTTTCTCTCTTTCCTCAATTTAATAATTATT
ATCTGTTGTTTACCAACTACTCAATTTCTCTTATAAGGGACTAAATATGTAGTCATCCTAAGGCGCATA
ACCATTTATAAAAAATCATCCTTCATTCTATTTTACCCTATCATCCTCTGCAAGACAGTCCTCCCTCAAA
CCCACAAGCCTTCTGTCTCACAGTCCCCTGGGCCATGGATCCTCACATCCCAATCCGCGGCCGCAATT
CGTAATCATGGTCATAGCTGTTTCTGTGTGAAATTGTTATCCGCTCACAATCCACACAACATACGAG
CCGGAAGCATAAAGTGTAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCT
CACTGCCCGCTTTCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGA
GAGGCGGTTTGCGTATTGGGCGC

The paragraph beginning on page 93, line 8, has been amended as follows:

pCG7-96 (SEQ ID NO:[41]40)

The paragraph beginning on page 94, line 12, has been amended as follows:

pG4HE (SEQ ID NO:[42]41)

The paragraph beginning on page 95, line 17, has been amended as follows:

10D1 VH(SEQ ID NO:16)

The paragraph beginning on page 95, line 27, has been amended as follows:

10D1 VK(SEQ ID NO:6)

The paragraph beginning on page 95, line 37, has been amended as follows:

4B6 VH(SEQ ID NO:18)

The paragraph beginning on page 95, line 47, has been amended as follows:

4B6 VK(SEQ ID NO:8)

The paragraph beginning on page 95, line 57, has been amended as follows:

1E2 VH(SEQ ID NO:22)

The paragraph beginning on page 96, line 7, has been amended as follows:

1E2 VK(SEQ ID NO:12)

IN THE CLAIMS:

31. (Amended) The human sequence antibody of claim 1, comprising heavy chain CDR1, CDR2, and CDR3 sequences, SYTMH (SEQ ID NO:27), FISYDGSNKHVYADSVKG (SEQ ID NO:33) and TGWLGPFDY (SEQ ID NO:[38]37), respectively, and light chain CDR1, CDR2, and CDR3 sequences, RASQSVSSSFLA (SEQ ID NO:25), GASSRAT (SEQ ID NO:30), and QQYGSSPWT (SEQ ID NO:35), respectively.

32. (Amended) The human sequence antibody of claim 1, comprising heavy chain CDR1, CDR2, and CDR3 sequences, SYGMH (SEQ ID NO:28), VIWYDGSNKYYADSVKG (SEQ ID NO:34) and APNYIGAFDV (SEQ